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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,475	12/30/2003	Masad J. Damha	MGU-0025	7556

7590 07/22/2005

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EXAMINER	
CHONG, KIMBERLY	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/748,475	DAMHA ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/04/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group 1 in the reply filed on 05/31/2005 is acknowledged. Claims 9-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicants have traversed the restriction requirement stating the "...oligonucleotides of Group I are not capable of separate use from the methods of Group II...", but provide no further evidence that the oligonucleotides of Group I would not be suitable as probes for *in situ* hybridization. Additionally, the methods of Group II could be practiced with an entirely different product, such as a single stranded antisense compound. Therefore, the restriction is still deemed proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other and further it is a burden to search these inventions in a single application.

THE RESTRICTION IS MADE FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to an oligonucleotide of Formula I, as shown in claim 1, wherein X1 and X2 are antiparallel strands forming a duplex and wherein Y1 and Y2 are 0 to 8 nucleotides in length, Y1 and Y2 are at least 2 to 8 nucleotides in length and Y1 and Y2 each independently contain a ribonucleic acid comprising SEQ ID NO: 1.

It is unclear how Y1 and Y2 can contain from 0, 1, 2 or 3 nucleotides *and* also independently contain a sequence with 4 nucleotides (SEQ ID NO: 1). The oligonucleotide having Formula I cannot contain regions Y1 and Y2 that are from 0-3 nucleotides and also contain the sequence provided as SEQ ID NO: 1.

Claim Rejections - 35 USC § 102 or 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

For purposes of prior art, the invention of the instant application is being interpreted to comprise a composition of Formula I, as shown in claim 1, wherein Y1 and Y2 can each be from 0 to 8 nucleotides in length.

Claims 1-7 are rejected under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Hannousch et al. (Document AE on Form PTO-1449 filed 10/04/2004).

Claim 1 is drawn to a composition for inhibiting the RNase H activity of a retroid virus reverse transcriptase comprising an inhibitory agent comprising two complementary regions linked by nucleotides comprising the sequence provided as SEQ ID NO: 1. Claims 2-5 limit claim 1 by reciting the complementary regions comprises 3',5'-linked ribonucleic acid, 2', 5'-linked nucleic acid, arabinoucleic acid, 2'-fluoro-arabinonucleic acid, locked nucleic acid, peptide nucleic acid or a combination thereof and the complementary region is comprised of deoxyribonucleic acid or ribonucleic acid. Claims 6-7 recites the complementary region comprises a 3-, 5'-linked ribonucleic acid that are 4 to 10 nucleotides in length, the Y nucleotides are a 3', 5'-linked tetranucleotide (SEQ ID NO:1).

Hannousch et al. teach a compound comprising two complementary strands 4 nucleotides in length, wherein the strands can be RNA or DNA or both and further wherein the strands are linked by a 5', 3'-linked loop identical 4 nucleotides in length comprising SEQ ID NO: 1. The compound taught by Hannousch et al. meets the structural limitation of claims 1-7 of the instant application and would be expected to inhibit the RNase H activity of a retroid virus reverse transcriptase. See, for example, MPEP 2112, which states "[w]here applicant claims a composition in terms of a function,

property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562.F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

Thus, the instant claims are anticipated or obvious over Hannousch et al.

Claims 1-5 are rejected under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Wasner et al. (Document AM on Form PTO-1449 filed 10/04/2004).

Claim 1 is drawn to a composition for inhibiting the RNase H activity of a retroid virus reverse transcriptase comprising an inhibitory agent comprising two complementary regions linked by nucleotides comprising the sequence provided as SEQ ID NO: 1. Claims 2-5 limit claim 1 by reciting the complementary regions comprises 3',5'-linked ribonucleic acid, 2', 5'-linked nucleic acid, arabinoucleic acid, 2'-fluoro-arabinonucleic acid, locked nucleic acid, peptide nucleic acid or a combination thereof and the complementary region is comprised of deoxyribonucleic acid or ribonucleic acid.

Wasner et al. teach a compound comprising two complementary strands 18-23 nucleotides in length, wherein the strands can be RNA or DNA or both and further

wherein the strands are 5', 3'-linked or 2', 5'-linked (see Figure 1 and Table 1). The compound taught by Wasner et al. meets the structural limitation of claims 1-5 of the instant application and would be expected to inhibit the RNase H activity of a retroid virus reverse transcriptase. See, for example, MPEP 2112, which states "[w]here applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

Thus, the instant claims are anticipated or obvious over Wasner et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andreola et al. (Document AA on Form PTO-1449 filed 10/04/2004), in view of Park et al. (Document AJ on Form PTO-1449 filed 10/04/2004) and in further view of Hannoush et al. (Document AE on Form PTO-1449 filed 10/04/2004).

Claim 1 is drawn to a composition for inhibiting the RNase H activity of a retroid virus reverse transcriptase comprising an inhibitory agent comprising two complementary regions linked by nucleotides comprising the sequence provided as SEQ ID NO: 1. Claims 2-5 limit claim 1 by reciting the complementary regions comprises 3',5'-linked ribonucleic acid, 2', 5'-linked nucleic acid, arabinoucleic acid, 2'-fluoro-arabinonucleic acid, locked nucleic acid, peptide nucleic acid or a combination thereof and the complementary region is comprised of deoxyribonucleic acid or ribonucleic acid. Claims 6-7 recites the complementary region comprises a 3-, 5'-linked ribonucleic acid that are 4 to 10 nucleotides in length, the Y nucleotides are a 3', 5'-linked tetranucleotide (SEQ ID NO:1). Claim 8 recites the composition is a cyclic structure.

Andreola et al. teach an oligonucleotide that is targeted to and inhibits the RNase H activity of a retroid virus reverse transcriptase (see page 10088, column 2 and Figure 2). Andreola et al. does not teach the oligonucleotide comprises antiparallel complementary oligonucleotide strands that associate to form a duplex of RNA or RNA and DNA and further are linked to a ribonucleotide having a sequence provided as SEQ ID NO:1.

Park et al. teach an oligonucleotide consisting of a sense and an antisense complementary region 22 nucleotides in length comprising RNA and DNA and further comprising two alkyl loop structures (see Figure 1).

Hannoush et al. teach a 2', 5'-linked ribonucleotide loop structure 4 nucleotides in length and identical to SEQ ID NO:1 (see Table 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the oligonucleotide taught by Andreola et al. for the circular oligonucleotides, taught by Park et al., to inhibit RNase H activity of a retroid virus reverse transcriptase. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the loop structures of the circular oligonucleotide taught by Park et al. with the 2', 5'-linked RNA loops, as taught by Hannoush et al.

One would have been motivated to use the circular oligonucleotides because Park et al. teach that circular oligonucleotides have increased nuclease resistance and cellular uptake compared to single stranded oligonucleotides (see page 954, column 1). One would have been motivated to substitute the alkyl loops of the circular oligonucleotide with a tetraloop comprising the sequences provided as SEQ ID NO:1 because Hannoush et al. teach hairpin structures comprising tetraloops are extremely stable and are important structural motifs for the design of synthetic nucleic acids (see page 12374, last paragraph).

Finally, one would have a reasonable expectation of success because Park et al. teach that circular oligonucleotide show increased resistance and uptake into cells and further have greater inhibitory effects compared to antisense oligonucleotides (see page 959, column 1 and Figure 6). Additionally, one would have a reasonable expectation of success because Hannoush et al. teach that a hairpin structure comprising a tetraloop is

stable and the increased stability is seen with duplexes having RNA or RNA and DNA (see Table 1).

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been

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Kimberly Chong
Examiner
Art Unit 1635